Objective
In double blind clinical trials, patients receive either an active formulation or a placebo without knowing what they get. To guarantee the reliability of the tests, it is important that active and placebo formulations have a similar taste so that this parameter will not influence the patients evaluation. The objective of this study was to investigate the optimal formulation of placebo in order to best match the taste of the real medicine.

Taste Assessment of Pharmaceutical Products with ASTREE Electronic Tongue

Working Principle of Electronic Tongue Compared to Human Taste

Electronic Tongue Analyzer

1. 16 or 48 position Autosampler (80 or 15 mL beakers)
2. Array of 7 electrochemical sensors (cross-selective & partially specific) + 1 reference electrode → potentiometric
3. Electronic unit for acquisition & autosampler control

Experimental Conditions & Samples
Six placebo formulations were prepared by adding 2 different bitter compounds (sodium benzoate and caffeine) at 3 distinct concentrations for each substance. For taste comparison purposes, a placebo without bitter compound and 2 active formulations (corresponding to 2 dosages: 500 mg and 1 g of active principle) were also prepared. Taste evaluation was performed using the ASTREE Electronic Tongue.

Sample set

<table>
<thead>
<tr>
<th>Sample designation</th>
<th>Formulation content</th>
</tr>
</thead>
<tbody>
<tr>
<td>A000</td>
<td>Active formulation 500 mg</td>
</tr>
<tr>
<td>A1</td>
<td>Active formulation 1g</td>
</tr>
<tr>
<td>P</td>
<td>Placebo without bitter agent</td>
</tr>
<tr>
<td>PNa80.05</td>
<td>Placebo + sodium benzoate 0.05 mg/mL</td>
</tr>
<tr>
<td>PNa80.25</td>
<td>Placebo + sodium benzoate 0.25 mg/mL</td>
</tr>
<tr>
<td>PNa80.5</td>
<td>Placebo + sodium benzoate 0.5 mg/mL</td>
</tr>
<tr>
<td>PCa0.05</td>
<td>Placebo + caffeine 0.05 mg/mL</td>
</tr>
<tr>
<td>PCa0.25</td>
<td>Placebo + caffeine 0.25 mg/mL</td>
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<td>Placebo + caffeine 0.5 mg/mL</td>
</tr>
</tbody>
</table>

E-Tongue Analytical Conditions
Sample volume: 25mL
Sample temperature: ambient
Time per analysis: 180 s
Acquisition time: 120 s

Taste Proximity Quantification

Fig.2: Distance between active medicine and each placebo formulation
To evaluate the taste differences and similarities between bitter placebo formulation and the medicine, the distance (Euclidian distance) between each bitter placebo and the active medicine was calculated. The shortest the distance, the lower the taste difference. Similarly, the lower the discrimination index, the lower the taste difference.

Based on the ASTREE Electronic Tongue measurements, it appears that for active dosages (500 mg and 1g), the lowest distance and discrimination index are obtained with the placebo containing 0.05 mg/mL of caffeine.

➡️ The placebo formulation containing 0.05 mg/mL of caffeine is the best match to both active medicines.

**Conclusion**

The taste of pharmaceutical formulations containing different bitter compounds at various concentrations could be rapidly tested using the ASTREE E-Tongue instrument. The study proved that it is possible to safely develop a taste matching placebo for consistent and reliable clinical trials.

**Taste Comparison of The Various Matrices**

The ASTREE measurement showed a high repeatability (Residual Standard Deviation < 1% on all sensors).

Instrumental results were plotted on a Principal Component Analysis (fig. 1) in order to visualize the taste map of all placebo and active formulations. This map shows the relative repartition and proximity of samples in terms of taste.

➡️ The various formulations are clearly differentiated.

➡️ Placebos containing sodium benzoate seem to be closer and to better match to the active references, especially the active formulation with 1 mg of API.